PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference P5104R1	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2004/011793	International filing date *(day/month/year)* 16 April 2004 (16.04.2004)	Priority date *(day/month/year)* 16 April 2003 (16.04.2003)]
International Patent Classification (IPC) or national classification and IPC [7] C07K 16/44, 14/47, G01N 33/53, A61P 35/00, C12N 15/12, 15/63, 15/09, A61K 31/7088, C07K 19/00, 16/46, A61K 39/395, G01N 33/574		
Applicant GENENTECH, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 15 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 21 October 2005 (21.10.2005)
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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

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From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/011793	16.04.2004	16.04.2003

International Patent Classification (IPC) or both national classification and IPC
C07K16/44, C07K14/47, G01N33/53, A61P35/00, C12N15/12, C12N15/63, C12N15/09, A61K31/7088, C07K19/00, C07K16/46, A61K39/395, G01N33/574

Applicant
GENENTECH, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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CORRECTED VERSION

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/011793

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 26-29,33-35,37,41,46-48,53,57-62,64-84 (all completely); 9-17,30-32,38,42-45,54-56 (all partially); 49-56,63 (with respect to IA)

because:

☒ the said international application, or the said claims Nos. 49-56,63 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 26-29,33-35,37,41,46-48,53,57-62,64-84 (all completely); 9-17,30-32,38,42-45,54-56 (all partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-25,36,39,40,49-52,63 (all completely); 30-32,38,42-45,54-56 (all partially)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14,17-19,22,23,25,38,39,40,42,50-52,54-56
	No:	Claims	15,16,20,21,24,30-32,36,43-45,49,63
Inventive step (IS)	Yes:	Claims	2-4,17-19
	No:	Claims	1,5-16,20-25,30-32,36,38-40,42-45,49-52,54-56,63
Industrial applicability (IA)	Yes:	Claims	1-25,30-32,36,38-40,42-45,63
	No:	Claims	

2. Citations and explanations

   see separate sheet

The numbering of the claims is not consistent. Number 3-5 have been assigned twice and a claim number 32 is missing. The claims have been renumbered consistently from 1 to 84 to which numbering it will be adhered during the international phase of this application.

Re item III

1.1 Claims 9-13, 15 and 16 refer to variants of antibodies which are solely defined by structural features, namely by amino acid sequences. As the term variant appears to be open-ended, the scope of said claims cannot be determined and the claims, thus, lack clarity (Art. 6 PCT). Consequently, the search of said variants was restricted to those which bind to the STOP-1 protein.

1.2 The same applies to dependent claim 14 (Art. 6 PCT).

1.3 Claim 17 refers to mAbs having the same biological characteristics as antibodies defined by the nucleic acids encoding them. It is not clear to which biological characteristics apart from the binding specificities to defined regions of the STOP-1 protein of said defined antibodies is referred to (Art. 6 PCT). Moreover, no characteristics of the said antibodies other than these binding specificities can be determined from the description of the present application. The search was, thus, limited to antibodies having the said binding specific ities.

1.4 Claims 54-56 relate inter alia to the use of a STOP-1 antagonist. It cannot be determined which compounds fall under the definition of a STOP-1 antagonist. Although claims 33, 34 and 65 define the binding site of the said antagonist, the compound is not defined in structural terms. As the said antagonist is not defined, the subject-matter of the said claims is also not defined and a meaningful search of these claims insofar as they relate to said antagonist was not possible (Art. 6 PCT). Consequently, these claims were only searched with respect to subject-matter excluding the said STOP-1 antagonist.

1.5 Claims 38-42 refer to a "stromal targeting agent". This agent is not defined by any structural features and it cannot be determined which compounds are covered by this

expression (Art. 6 PCT). A meaningful search over the whole scope of said claim is, thus, not possible and the search has been restricted to the specific embodiments of stromal targeting agents given at page 48, l. 27-28 of the instant description.

1.6 Claim 30 refers to nucleic acids encoding the antibody according to any of claims 1-21. However, these can only be directly derived from claim 19 and indirectly from the amino acid sequences proposed by claims 15 and 16 insofar as they do not refer to variants thereof which again introduce unclarity with respect to the said nucleic acid sequences (Art. 6 PCT). The other claims refer to antibodies which are defined by functional features or by amino acid sequences whose positions in the antibodies are not clearly defined. For these antibodies it is not possible to determine which nucleic acids encode them. The search of claim 30, therefore, has been limited to nucleic acids encoding antibodies as defined by claims 14, 16 and 19. The same considerations also apply to claims 31, 32 and 43-45 referring to the said nucleic acid.

1.7 The substantive examination will be restricted to the said searched subject-matter (cf. III 1.1 -1.6) (R. 66.1(e) PCT).

2. Claims 49-56 and 63 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re item IV

The International Preliminary Examination Authority (IPEA) concurs with the observation as to lack of unity raised by the International Search Authority (ISA) and identifies the following inventions:

Invention 1 (claims 1-25, 36, 39, 40, 49-52, 63 (all completely); 30-32, 38, 42-45, 54-56 (all partially)):

A monoclonal antibody (mAb) that specifically binds to an oligomeric form of human

STOP-1; a mAb that specifically binds to amino acids 33-52 or 33-53 of human STOP-1; a mAb that specifically binds to amino acids 94-243 of human STOP-1; a mAb comprising the three amino acid sequences defined in any of claims 5, 9 and 10; a mAb comprising the amino acid sequence of the heavy chain of any of Fig. 27-31 or 34; a mAb having the biological characteristics of a mAb selected from S4, S7, S9, S16, F5 and 6B12; a mAb that specifically binds to STOP-1, wherein the binding of the mAb can be inhibited by a second mAb selected from S4, S7, S9, S16, F5 and 6B12; a mAb that specifically binds to STOP-1, wherein the mAb comprises the light and heavy chain sequences of any S4, S7, S9, S16, F5 and 6B12; a nucleic acid molecule encoding any of said mAbs; a vector comprising said nucleic acid molecule; a host cell comprising said nucleic acid molecule; a composition comprising one of said mAbs; a composition comprising the said nucleic acid molecule; a method for producing any of said mAbs using the said nucleic acid; a method for diagnosing or monitoring a tumour of a patient; a method of inhibiting the growth of a tumour that overexpresses STOP-1 comprising administering to a patient the said mAb composition; a method for determining the presence of a STOP-1 polypeptide in a sample

Invention 2 (claims 26, 27, 57-59 (all completely); 30-32, 37, 38, 41-45, 54-56, 64 (all partially)):

A STOP-1 polypeptide variant comprising a STOP-1 polypeptide that cannot be secreted; a nucleic acid encoding the said polypeptide; a vector comprising the said nucleic acid; a host cell comprising the said nucleic acid; a composition comprising said polypeptide; a composition comprising said nucleic acid; a method of producing a STOP-1 polypeptide using the said nucleic acid; a method of inhibiting the growth of a tumour that overexpresses STOP-1 comprising administering to a patient the said composition; a method of inhibiting the growth of a cell that overexpresses STOP-1 comprising the step of inhibiting the secretion of STOP-1 from the cell; an article of manufacture comprising a modified STOP-1 polypeptide or a STOP-1 polypeptide variant

Invention 3 (claims 28, 29, 60 (all completely); 30-32, 37, 41-45, 54-56, 64 (all partially)):

A STOP-1 polypeptide variant that cannot disulfide bind with another STOP-1; a nucleic acid encoding the said polypeptide; a vector comprising the said nucleic acid; a host cell comprising the said nucleic acid; a composition comprising said polypeptide; a composition comprising said nucleic acid; a method of producing a STOP-1 polypeptide using the said nucleic acid; a method for preventing disulfide binding between STOP-1 molecules; a method of inhibiting the growth of a tumour that overexpresses STOP-1 comprising administering to a patient the said composition; an article of manufacture comprising a modified STOP-1 polypeptide or a STOP-1 polypeptide variant;

Invention 4 (claims 46-48 (all completely)):

A method for producing a STOP-1 polypeptide using a mammalian cell that is deficient in proteoglycan synthesis

Invention 5 (claims 61, 62 (all completely)):

A method for cleaving STOP-1 comprising the step of incubating STOP-1 with a protease

Invention 6 (claims 66-68 (all completely)):

A method of inducing cell migration in vitro comprising the administration of a STOP-1 polypeptide; a method of testing the activity of a candidate antagonist or agonist of STOP-1 on cell migration

Invention 7 (claims 70-84 (all completely)):

A composition comprising an immunoadhesin that comprises a STOP-1 polypeptide and an Fc portion of an antibody; a composition comprising a molecule that potentiates the binding of a STOP-1 polypeptide to a cell surface; an article of manufacture comprising said STOP-1 potentiator or said immunoadhesin; a method of inducing angiogenesis using said STOP-1 potentiator or said immunoadhesin; a

method for evaluating/identifying compounds affecting the binding of STOP-1 to cells.

The reasons for the obejction being as follows:

a) The only identifiable technical feature that all inventions have in common is that they relate to the STOP-1 protein.

b) However, said feature cannot represent a special technical feature in the sense of R. 13.2 PCT as it is known in the art. WO 02/071928 (D2) discloses the STOP-1 protein (M450) as well as the nucleic acid encoding it, and teaches M450 overexpression in ovarian cancer (p. 39, para.2; p. 50, para. 2 - p. 64, para. 2; p. 72, para. 3 - p. 95, para. 3; tables 1 and 2; claim 1). Also disclosed are antibodies specific for the said STOP-1 protein and pharmaceutical compositions comprising the said antibodies, as well as methods of diagnosing and monitoring ovarian cancer by determining M450 expression by e.g. ELISA, namely wherein an increased expression of M450 is indicative of ovarian cancer. EP 1179540 (D4) discloses the secretory STOP-1 protein (TGC-628), the nucleic acid encoding it, antibodies specific thereto and compounds that inhibit its activity (example 7; claims 1-8; SEQ ID No. 2). WO 02/16602 (D1) discloses the STOP-1 protein as well as the nucleic acid encoding it (DNA76393-1664) and teaches that STOP-1 is a tumour associated antigen (p. 7, l. 15 - p. 17, l. 15; Fig. 7; SEQ ID No. 7). Disclosed are methods of diagnosing the presence of a tumour in a mammal based on the expression level of STOP-1. Furthermore, D1 teaches a method of treating a mammal having a tumour comprising cells that express STOP-1 by administering inter alia an antibody that binds to STOP-1.

c) In view of the prior art represented by D1, D2 and D4 the problems of the underlying application can be formulated as i) the provision of further STOP-1 specific antibodies as well as of further uses thereof; ii) the provision of STOP-1 variants as well as of uses thereof; iii) the provision of further methods using STOP-1; iv) the provision of compounds affecting the activity of STOP-1.

d) Each of the inventions listed above represents an independent solution

concerning one of the foregoing problems of the underlying application. Solution 1 is the provision of mAbs binding to the oligomeric form of human STOP-1 as well as of uses thereof. Solution 2 is the provision of a STOP-1 polypeptide variant that cannot be secreted as well as of uses thereof. Solution 3 is the provision of a STOP-1 polypeptide variant that cannot disulfide bind with another STOP-1 as well as of uses thereof. Solution 4 is a method of producing a STOP-1 polypeptide. Solution 5 is a method for cleaving STOP-1. Solution 6 is a method of inducing cell migration involving STOP-1 as well as of testing candidate antagonists or agonists of STOP-1 for their effect on cell migration. Solution 7 is the provision of compounds affecting STOP-1 binding to cells as well as of uses thereof and of methods for evaluating/identifying the said compounds.

e) In view of the fact that the STOP-1 protein is known from the prior art as well as antibodies thereto and methods using STOP-1, namely to detect and treat tumours expressing STOP-1; due to the fact that the STOP-1 variants according to solution 2 and 3 do not share any structural feature other than known STOP-1 amino acid sequences; and due to the fact that no other technical features can be distinguished which, in the light of the prior art could be regarded as special technical features common to the above solutions, the IPEA is of the opinion that there is no single inventive concept in the sense of R. 13.1 PCT underlying the 7 solutions contained in the present application. Consequently, there is a lack of unity, and different inventions have to be formulated as different subjects as done on the communication pursuant to Art. 17(3)(a) PCT.

f) The ISA has searched the first invention (claims1-25, 33-36, 39, 40, 49-53, 63, 65, 69 (completely); 30-32, 38, 42-45, 54-56, 64 (all partially)).

g) The substantive examination will only be carried out for those parts of the application for which a search report has been established (R. 66.1(e) PCT).

Re item V

1. Reference is made to the follwoing documents:

   D1: WO 02/16602 A 28 February 2002 (2002-02-28)
   D2: WO 02/071928 A 19 September 2002 (2002-09-19)
   D3: WO 92/09690 A 11 June 1002 (1992-06-11)
   D4: EP-A-1 179 540 13 February 2002 (2002-02-13)
   D4: HOLT L J ET AL: "Domain antibodies: proteins for therapy" TRENDS IN BIOTECHNOLOGY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 11, November 2003 (2003-11), pages 484-490

2.1 D1 teaches a method of diagnosing the presence of a tumour on the bases of detecting the expression level of the STOP-1 polypeptide in a patient's tissue sample in comparison to the STOP-1 expression level in a control sample (p. 16, l. 25-35). The subject-matter of claims 49 and 63, thus, lacks novelty over D2 (Art. 33(2) PCT).

D2 teaches a method of diagnosing ovarian cancer comprising determining an overexpression of STOP-1 in a patient's sample as compared to a control non-ovarian sample by means of e.g ELISA (claim 1, p. 87, last para. - p. 95, 3rd para.; Tab. 1 and 2). The subject-matter of claim 49 and 63, thus, lacks novelty over D2 (Art. 33(2) PCT).

2.2 D4 discloses a monoclonal antibody comprising a heavy chain which is a variant of the heavy chains according to Fig. 30-32 and 34 (Example 11; Fig. 11; claim 46), thereby anticipating the novelty of claim 15 (Art. 33(2) PCT).

2.3 D4 also discloses the nucleic acid of said antibody, a vector comprising said nucleic acid molecule and a host cell comprising said nucleic acid molecule (supra). Hence, the disclosure of D4 is novelty-destroying for the subject-matter of claims 30-32 (Art. 33(2) PCT).

2.4 The only technical features of the compositions according to claims 36 and 43 are the antibody and the nucleic acid, respectively. These are known from D4 (supra) which, thus, destroys the novelty of said claims (Art. 33(2) PCT).

2.5 The antibody of D4 is produced by culturing bacterial cells comprising the nucleic acid encoding it (Example 11). D4, thus, anticipates the novelty of claim 44 (Art. 33(2) PCT).

2.6 The additional features according to claims 16, 20, 21, 24 and 45 are also disclosed in D4 (supra) and, thus, do not establish novelty (Art. 33(2) PCT).

2.7 The subject-matter of claims 1-14, 17-19, 22, 23, 25, 38-40, 42, 50-52 and 54-56 is considered novel as the combinations of features suggested by these claims are not known in the art (Art. 33(2) PCT).

3.1 D1-D3 disclose antibodies specific to STOP-1 (D1: p. 10, l. 9 - p. 11, l. 5; D2: p. 39, l. 8-10 and p. 56, l. 20 - p. 64, l. 13; D3: claim 3). Using standard expression systems for the full length STOP-1 cDNA disclosed in any of D1-D3 will produce oligomeric forms of STOP-1, and antibodies raised thereagainst by means of routine techniques will bind to these oligomeric forms. Hence, the subject-matter of claim 1 does not involve an inventive step (Art. 33(3) PCT).

3.2 Claims 5-13 refer to antibodies comprising three amino acid sequences regardless whether these sequences are contained in CDRs or in framework regions. Thus, the sequences used to define the claimed antibodies do not confer any specificity to the said antibodies. Hence, the technical problem to be solved by these claims has to be regarded as the provision of antibodies having these sequences. In view of the fact that these sequences do not impose a specificity, they are considered arbitrary selections out of equally likely alternatives. Consequently, claims 5-13 are not considered to involve an inventive step (Art. 33(3) PCT).

3.3 Claim 14 specifies the sequences of claims 5-13 to be within the CDRs of a heavy chain. No support is provided that every possible combination of CDRs proposed by claim 5 taken in combination with claim 14 has a specificity for STOP-1 (Art. 6 PCT). In fact, the only antibodies having this specificity are antibodies whose heavy chains are defined by a combination of any of claims 9-3 with claim 14. Consequently, the problem of providing antibodies specific for STOP-1 is not considered to be solved by all antibodies falling under the scope of claim 14. Hence, no inventive step can be

acknowledged (Art. 33(3) PCT).

3.4 The subject-matter of claim 51 differs from either D1 or D2 by the antibody suggested. The use of the non-inventive antibody (cf. V 3.1) in the method of either D1 or D2 (cf. V 2.1), however, does not establish an inventive step. Therefore, claim 51 does not involve an inventive step (Art. 33(3) PCT).

3.5 D1 teaches a method of treating a patient having a STOP-1 expressing tumour by administering a STOP-1 specific mAb (p. 15, l. 20-28). Claim 54 is distinguished from D1 by the antibody used. This antibody, however, is not inventive (cf. V 3.1) and, thus, its use does not establish an inventive step for said claim (Art. 33(3) PCT).

3.6 The additional features suggested by claims 22, 23, 25, 38-40, 42, 50, 52, 55 and 56 involve routine modifications which do not result in any unforeseeable technical effect. These claims are therefore not considerd inventive (Art. 33(3) PCT).

3.7 The subject-matter of claim 2 is distinguished from any of D1-D3 in that the epitop of the antibody are amino acids 33-52 or 33-53 of STOP-1. The technical effect is that said antibody allows the detection of STOP-1 fragments that do not oligomerise. The technical problem thus resides in providing a STOP-1 specific mAb allowing the determination of STOP-1 fragments that do not oligomerise. The solution according to claim 2 is not obvious over the prior art and thus involves an inventive step (Art. 33(3) PCT).

3.8 A similar argumentation applies for claim 3 and its dependent claim 4 which provide an antibody that allows the detection of STOP-1 fragments that are capable of oligomerisation. An inventive step is, hence, acknowledged for the subject-matter of claims 3 and 4 (Art. 33(3) PCT).

3.9 For the foregoing considerations (cf. V 3.7 and 3.8) also claims 17-19 are considered to involve an inventive step (Art. 33(3) PCT).

4.1 For the assessment of the present claims 49-52, 54-56 and 63 on the question whether they are industrially applicable, no unified criteria exist in the PCT

Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment..

4.2 Industrial applicability of the subject-matter of claims 1-25, 30-32, 36, 38-40, 42-45 and 63 is acknowledged (Art. 33(4) PCT).

5.1 Claim 16 refers to the amino acid light chain sequence of Fig. 34. This figure, however, does not contain an amino acid sequence of a light chain, thereby obscuring the scope of said claim (Art. 6 PCT).

5.2 Claim 39 refers to an antagonist which, however, is not mentioned in the antecedent of said claim, thereby creating unclarity (Art. 6 PCT). The expression was interpreted as referring to the monoclonal antibody of claim 36. In this interpretation claim 39 is indistinguishable from claim 40 and, thus, superfluous (Art. 6 PCT, conciseness).

5.3 Claim 56 refers to "round cell tumours" and "vascular cancer" which are vague and do not define a clear disease, thereby rendering the scope of said claim unclear (Art. 6 PCT).